

AD _____

Award Number: DAMD17-01-1-0515

TITLE: PET Imaging of Breast Cancer Using F-18 Labeled Choline
Analog

PRINCIPAL INVESTIGATOR: Mary Scott Soo, M.D.

CONTRACTING ORGANIZATION: Duke University Medical Center
Durham, NC 27710

REPORT DATE: November 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20040608 131

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 074-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503				
1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE November 2003		3. REPORT TYPE AND DATES COVERED Annual (1 Nov 2002 - 31 Oct 2003)
4. TITLE AND SUBTITLE PET Imaging of Breast Cancer Using F-18 Labeled Choline Analogs			5. FUNDING NUMBERS DAMD17-01-1-0515	
6. AUTHOR(S) Mary Scott Soo, M.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Duke University Medical Center Durham, NC 27710 E-Mail: Soo000002@mc.duke.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) No Abstract Provided				
14. SUBJECT TERMS positron emission tomography(PET); positron emission mammography(PEM); breast cancer; fluorocholeline				15. NUMBER OF PAGES 6
				16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

Table of Contents

Cover.....	1
SF 298.....	2
Table of Contents.....	3
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	5
Reportable Outcomes.....	5
Conclusions.....	5
References.....	5
Appendices.....	6

TITLE: PET Imaging of Breast Cancer using F-18 Labeled Choline Analogs

Principal Investigator: Mary Scott Soo, M.D.

Department of Radiology
Box 3808
South Hospital
Duke University Medical Center
Durham, N.C. 27710
919-684-7829

Co-investigators: Timothy DeGrado Ph.D., Eric L. Rosen M.D., Tim Turkington, Ph.D., R. Edward Coleman M.D., Lesa Kurylo

INTRODUCTION: Mammography has proven effective for reducing mortality from breast cancer, however detection of some lesions is limited by dense breast tissue that obscures the tumor, and the specificity of mammography is low. Functional imaging with positron emission tomography (PET) may help improve detection and diagnosis of breast cancer, although, the diagnostic accuracy of primary breast tumors has been found to be hindered by low glycolytic rates, and nonspecific uptake by nonmalignant breast tissue. Imaging with fluorocholine (FCH) may help to overcome these limitations. An efficient and practical synthesis of FCH has been developed at our institution. The purpose of the study is to evaluate the potential utility of F-18 labeled choline (FCH) as a positron emission tomography (PET) radiotracer for detection and diagnosis of breast cancer in women with highly suspicious breast lesions. Our goals are to determine: 1) the correlation between FCH uptake in primary breast cancer tumors and the histologic tumor type from subsequent pathology; 2) how FCH uptake in breast cancer tumors compares to F-18 2-fluoro-2-deoxy-glucose (FDG) (which is the current standard cancer imaging agent for PET) uptake in breast cancer tumors; and 3) if FCH can improve local staging of the breast in patients with recently diagnosed breast cancer (invasive or *in situ*).

BODY: To date, no subjects have been recruited or enrolled into this study, and the project has received a second 12-month no cost time extension. In order to satisfy all the requirements of the Human Subjects Protection Scientist for Human Subjects Approval prior to beginning the study, it has been required that we apply for an IND from the FDA for the experimental drug fluorocholine. The radiotracer FCH is an investigational radiotracer imaging agent currently produced under the sanction of the Radioactive Drug Research Committee (RDRC) and IRB at Duke University. To date, no adverse events have occurred in our experience with PET imaging using flurocholine analogs in

approximately 25 patients. Regarding the IND status, we are developing an automated synthesis system for making the FCH, and information on this process was requested and is pending for the IND. We are currently still working on the synthesis modules for the fluorocholine, and the hardware has been completed. Programming and optimization of the system is underway. Following completion of the automated synthesis process, and approval of use of the fluorocholine by the FDA, phase 1 studies will be underway. When we have approval for phase 2 studies, we will then finalize the Human Subjects Approval and our Institutional Review Board approval, and should then be able to recruit patients into the study as previously outlined.

KEY RESEARCH ACCOMPLISHMENTS: Progress toward IND final approval has occurred, including development of the automated synthesis system for the fluorocholine, with completion of the hardware components. Programming and optimization of the system is underway, and we have completed the standard operating procedure manual for this process. Phase 1 studies should be underway soon, with anticipated completion in spring 2004.

REPORTABLE OUTCOMES: Not applicable, pending IND approval as above

CONCLUSIONS: Following FDA approval of the fluorocholine as an investigational new drug, Human Subjects and IRB final approval for the study, 20 patients will be recruited into the study. Patients will be imaged on an experimental dedicated PET mammography unit recently developed for Duke University Medical Center, which has been successfully used to image and identify breast carcinomas seen at mammography. Each subject will be scanned with FCH-PET and FDG-PET on different days within a period of 2 weeks, at least one day apart. Imaging will proceed after the radiotracer is administered and an uptake period of approximately 5 minutes for FCH and 45 minutes for FDG has elapsed. Data acquisition will last up to 5 minutes per imaging position. The corresponding mammographic films obtained for routine clinical evaluation will be subsequently digitized and transferred to and displayed on the same computer as the digital PEM images. Findings at PEM imaging with FCH and FDG will be reviewed and compared, and correlated with the mammograms and histology of the known breast cancer.

REFERENCES:

DeGrado TR, Baldwin SW, Wang S, Orr MD, Liao RP, Friedman HS, Reiman RE, Price DT, Coleman RE. Synthesis and evaluation of ¹⁸F-labeled choline analogs as oncologic PET tracers. J Nucl Med, In press.

DeGrado TR, Coleman RE, Wang S, Baldwin SW, Orr MD, Robertson CN, Polascik TJ, Reiman RE, Price DT. Synthesis and evaluation of ¹⁸F-labeled choline as an oncologic tracer for positron emission tomography: initial findings in prostate cancer. Cancer Res, 61:110-117, 2001.

DeGrado TR, Orr MD, Wang SW, Price DT, Coleman RE, Baldwin SW. Structure-activity relationships for uptake of 18F-labeled choline analogs by prostate cancer models. Proceedings of the 4th International Symposium on Radiohalogens, Whistler BC, Canada, September 9-13, 2000.

DeGrado TR, RE Coleman, Baldwin SW, Orr MD, Wang S, Liao RP, Price DT. F-18 Labeled Choline Analogs as PET Imaging Probes of Prostate Cancer, J Urol, In press.

DeGrado TR, Coleman RE, Wang S, Price DT, Orr MD, Baldwin SW. Structure-activity relationships of 18F-labeled choline analogs for oncologic PET imaging. J Nucl Med 2001; 42:149P.

DeGrado TR, Baldwin SW, Orr MD, Wang S, Liao RP, Price DT, Coleman RE. Preliminary metabolic studies with [18F]fluorocholine (FCH), a novel oncologic probe for PET. J Nucl Med 2001; 42:149P.

APPENDICES: Not applicable